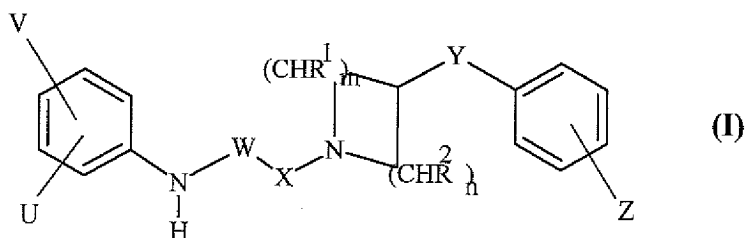


Amendments to the Claims

The listing of claims will replace all prior versions, and listing of claims in the application.

1. (Currently Amended) A compound comprising a structure of formula (I):



wherein:

V and U: ~~independently are hydrogen, halogen, hydroxyl, cyano, nitro, amino, C₁-C₄-alkylamino, halogen substituted C₁-C₄-alkylamino, arylamino, halogen substituted arylamino, aralkylamino, halogen substituted aralkylamino, C₁-C₄-alkylsulfonamido, halogen substituted C₁-C₄-alkylsulfonamido, C₁-C₄-alkanoylamido, halogen substituted C₁-C₄-alkanoylamido, arylsulfonamido, C₁-C₄-alkylsulfonyloxy, carboxyl, carbamoyl, trifluoromethyl, trifluoromethoxy, C₁-C₄-alkyl-SO₂-NH-CH₂-, C₁-C₄-alkyl-SO₂-NH-, NH₂-(CH₂)₁₋₄-SO₂-NH-, NH₂-(CH₂)₁₋₄-(CO)-NH-, NH₂-SO₂-, CHO-, CH₂-NH₂-, hydroxymethyl, C₁-C₄-alkyl, C₁-C₄-alkoxy methyl, halogenmethyl, tetrazolyl, C₁-C₄-alkoxy, amino substituted C₁-C₄-alkoxy, C₁-C₄-alkoxycarbonyl, amino substituted C₁-C₄-alkoxycarbonyl, C₁-C₆-alkanoyloxy, amino substituted C₁-C₆-alkanoyloxy, phenyl, amino substituted phenyl or acetylamino; or~~

together form a group that contains one or more heteroatoms, and that taken together with one or more:

- (a) hydrogen atoms;
- (b) carbon atoms;
- (c) -CH= groups;
- (d) -CH₂- groups; or
- (e) additional heteroatoms of the same or different type;

or any combination thereof, form a 4-7 membered homocyclic or heterocyclic ring, wherein the homocyclic or heterocyclic ring may combine with the phenyl group to form a bicyclic ring, and wherein the homocyclic or heterocyclic ring or the bicyclic ring may

contain one or more oxo, thioxo, amino, mercapto, trifluoromethyl, C₁-C₄ alkyl, =S or -SH groups;

W: is -CO-, -CH₂- or -CH₂-(C₁-C₄ alkyl)-;

X: is -CO-;

Y: is -O-, C₁-C₄ alkylene, C₁-C₄ alkynylene, cycloalkylene, aminocarbonyl, -NH-, -N(C₁-C₄ alkyl)-, -C₁-C₄ alkylene-N(C₁-C₄ alkyl)-, -CH₂O-, -CH(OH)- or -OCH₂-;

Z: is hydrogen, halogen, nitro, amino, C₁-C₄ alkyl, C₁-C₄ alkoxy, cyano, trifluoromethyl, hydroxyl or carboxyl;

R^I and R²: are hydrogen, or together form a C₁-C₃ bridge; and

n and m: independently are 0-3, wherein n and m cannot each be 0;

or an optical antipode, racemate or pharmaceutically-acceptable salt thereof.

2. (Original) The compound of claim 1 wherein -(CHR¹)_m and -(CHR²)_n are each -CH₂-CH₂-.

3. (Original) The compound of claim 2 wherein W is -CH₂-.

4. (Original) The compound of claim 2 wherein W is -CO-.

5. (Canceled)

6. (Original) The compound of claim 2 wherein V and U together form a group that contains one or more heteroatoms, and that taken together with one or more:

(a) hydrogen atoms;

(b) carbon atoms;

(c) -CH= groups;

(d) -CH₂- groups; or

(e) additional heteroatoms of the same or different type;

or any combination thereof, form a 4-7 membered homocyclic or heterocyclic ring, wherein the homocyclic or heterocyclic ring may combine with the phenyl group to form a bicyclic ring, and wherein the homocyclic or heterocyclic ring or the bicyclic ring may contain one or more oxo, thioxo, amino, mercapto, trifluoromethyl, C₁-C₄ alkyl, =S or -SH groups.

7. (Original) The compound of claim 6 wherein the homocyclic or heterocyclic ring combines with the phenyl group to form a bicyclic ring.

8. (Original) The compound of claim 6 wherein the homocyclic or heterocyclic ring is morpholine, pyrrole, pyrrolidine, oxo-pyrrolidine, thioxo-pyrrolidine, pyrazole, pyrazolidine, imidazole, oxo-imidazole, thioxo-imidazole, imidazolidine, oxo-imidazolidine, thioxo-imidazolidine, 1,4-oxazine, oxazole, oxazolidine, oxo-oxazolidine, thioxo-oxazolidine or 3-oxo-1,4-oxazine.

9. (Canceled)

10. (Original) The compound of claim 3 wherein V and U together form a group that contains one or more heteroatoms, and that taken together with one or more:

(a) hydrogen atoms;

(b) carbon atoms;

(c) -CH= groups;

(d) -CH₂- groups; or

(e) additional heteroatoms of the same or different type;

or any combination thereof, form a 4-7 membered homocyclic or heterocyclic ring, wherein the homocyclic or heterocyclic ring may combine with the phenyl group to form a bicyclic ring, and wherein the homocyclic or heterocyclic ring or the bicyclic ring may contain one or more oxo, thioxo, amino, mercapto, trifluoromethyl, C₁-C₄ alkyl, =S or -SH groups.

11. (Original) The compound of claim 10 wherein the homocyclic or heterocyclic ring is morpholine, pyrrole, pyrrolidine, oxo-pyrrolidine, thioxo-pyrrolidine, pyrazole, pyrazolidine, imidazole, oxo-imidazole, thioxo-imidazole, imidazolidine, oxo-imidazolidine, thioxo-imidazolidine, 1,4-oxazine, oxazole, oxazolidine, oxo-oxazolidine, thioxo-oxazolidine or 3-oxo-1,4-oxazine.

12. (Canceled)

13. (Original) The compound of claim 4 wherein V and U together form a group that contains one or more heteroatoms, and that taken together with one or more:

(a) hydrogen atoms;

(b) carbon atoms;

(c) -CH= groups;

(d) -CH₂- groups; or

(e) additional heteroatoms of the same or different type;

or any combination thereof, form a 4-7 membered homocyclic or heterocyclic ring, wherein the homocyclic or heterocyclic ring may combine with the phenyl group to form a bicyclic ring, and wherein the homocyclic or heterocyclic ring or the bicyclic ring may contain one or more oxo, thioxo, amino, mercapto, trifluoromethyl, C₁-C₄ alkyl, =S or -SH groups.

14. (Original) The compound of claim 13 wherein the homocyclic or heterocyclic ring is morpholine, pyrrole, pyrrolidine, oxo-pyrrolidine, thioxo-pyrrolidine, pyrazole, pyrazolidine, imidazole, oxo-imidazole, thioxo-imidazole, imidazolidine, oxo-imidazolidine, thioxo-imidazolidine, 1,4-oxazine, oxazole, oxazolidine, oxo-oxazolidine, thioxo-oxazolidine or 3-oxo-1,4-oxazine.

15. (Currently Amended) The compound of claim 1 wherein the compound is:
2-[4-(4-fluoro-benzyl)-piperidin-1-yl]-2-oxo-N-(2-oxo-2,3-dihydro-1H-indol-5-yl)-acetamide;

2-[4-(4-fluoro-benzyl)-piperidin-1-yl]-2-oxo-N-(2-oxo-2,3-dihydro-benzoxazol-6-yl)-acetamide;

2-[4-(4-fluoro-benzyl)-piperidin-1-yl]-2-oxo-N-(2-oxo-2,3-dihydro-1H-benzimidazol-5-yl) acetamide;

2-(4-benzyl-piperidin-1-yl)-2-oxo-N-(2-oxo-2,3-dihydro-1H-indol-5-yl)-acetamide;

2-(4-benzyl-piperidin-1-yl)-2-oxo-N-(2-oxo-2,3-dihydro-1H-benzimidazol-5-yl)-acetamide;

2-(4-benzyl-piperidin-1-yl)-2-oxo-N-(2-oxo-2,3-dihydro-benzoxazol-6-yl)-acetamide;

5-{2-[4-(4-fluoro-benzyl)-piperidin-1-yl]-2-oxo-ethylamino}-1,3-dihydro-benzimidazol-2-one;

6-{2-[4-(4-fluoro-benzyl)-piperidin-1-yl]-2-oxo-ethylamino}-3H-benzoxazol-2-one;

2-[4-(4-methylbenzyl)-piperidin-1-yl]-2-oxo-N-(3-oxo-3,4-dihydro-2H-benzo[1,4]oxazin-7-yl) acetamide;

2-[4-[4-methyl-benzyl)-piperidin-1-yl]-2-oxo-N-(2-oxo-2,3-dihydro-1H-indol-5-yl)-acetamide;

2-[4-(4-chloro-phenoxy)-piperidin-1-yl]-2-oxo-N-(2-oxo-2,3-dihydro-1H-benzimidazol-5-yl) acetamide;

2-[4-(4-chloro-phenoxy)-piperidin-1-yl]-2-oxo-N-(2-oxo-2,3-dihydro-benzoxazol-6-yl) acetamide;

2-[4-(4-chloro-benzyl)-piperidin-1-yl]-2-oxo-N-(2-oxo-2,3-dihydro-benzoxazol-6-yl)-acetamide;

2-[4-(4-chloro-benzyl)-piperidin-1-yl]-2-oxo-N-(2-oxo-2,3-dihydro-1H-benzimidazol-5yl) acetamide;

2-oxo-N-(2-oxo-2,3-dihydro-benzoxazol-6-yl)-2-(4-p-tolyloxy-piperidin-1-yl)-acetamide;

2-oxo-N-(2-oxo-2,3-dihydro-1H-benzimidazol-6-yl)-2-(4-p-tolyloxy-piperidin-1-yl)-acetamide;

2-[4-(4-chloro-benzyl)-piperidin-1-yl]-2-oxo-N-(2-oxo-2,3-dihydro-1 H-indol-5-yl)-acetamide;

6-[2-(4-benzyl-piperidin-1-yl)-2-oxo-ethylamino]-3H-benzoxazol-2-one;

2-(4-benzyl-piperidin-1-yl)-N-(2-mercapto-3H-benzimidazol-5-yl)-2-oxo-acetamide;

2-(4-benzyl-piperidin-1-yl)-2-oxo-N-(2-oxo-2,3-dihydro-benzothiazol-6-yl)-acetamide;

2-[4-(4-fluoro-benzyl)-piperidin-1-yl]-N-(2-mercapto-3H-benzimidazol-5-yl)-2-oxo-acetamide;

2-[4-(4-fluoro-benzyl)-piperidin-1-yl]-2-oxo-N-(2-oxo-2,3-dihydro-benzothiazol-6-yl) acetamide;

2-oxo-N-(2-oxo-2,3-dihydro-benzothiazol-6-yl)-2-(4-p-tolyloxy-piperidin-1-yl)-acetamide;

N-(2-mercapto-3H-benzimidazol-5-yl)-2-(4-p-tolyloxy-piperidin-1-yl)-2-oxo-acetamide;

2-[4-(4-methyl-benzyl)-piperidin-1-yl]-2-oxo-N-(2-oxo-2,3-dihydro-benzoxazol-6-yl] acetamide;

2-[4-[4-methoxy-benzyl)-piperidin-1-yl]-2-oxo-N-(2-oxo-2,3-dihydro-benzoxazol-6-yl) acetamide;

2-[4-[3-methoxy-benzyl)-piperidin-1-yl]-2-oxo-N-(2-oxo-2,3-dihydro-benzoxazol-6-yl) acetamide;

2-[4-[3-methyl-benzyl)-piperidin-1-yl]-2-oxo-N-(2-oxo-2,3-dihydro-benzoxazol-6-yl) acetamide;

2-[4-(4-cyano-benzyl)-piperidin-1-yl]-2-oxo-N-(2-oxo-2,3-dihydro-benzoxazol-6-yl)acetamide;

2-[4-[3-fluoro-benzyl)-piperidin-1-yl]-2-oxo-N-(2-oxo-2,3-dihydro-benzoxazol-6-yl)acetamide;

2-[4-(2,4-difluoro-benzyl)-piperidin-1-yl]-2-oxo-N-(2-oxo-2,3-dihydro-benzoxazol-6-yl) acetamide;

6-(2-[4-(4-methyl-benzyl)-piperidin-1-yl]-2-oxo-ethylamino}-3H-benzoxazol-2-one;

2-[4-(3,4-difluoro-benzyl)-piperidin-1-yl]-2-oxo-N-(2-oxo-2,3-dihydro-benzoxazol-6-yl) acetamide;

2-[4-(4-methyl-benzyl)-piperidin-1-yl]-2-oxo-N-(2-oxo-1,2,3,4-tetrahydro-tetrahydro-quinolin-6-yl acetamide;

2-[4-(4-methyl-benzyl)-piperidin-1-yl]-2-oxo-N-(2-oxo-2,3-dihydro-benzothiazol-6-yl) acetamide;

2-[4-(4-chloro-phenoxy)-piperidin-1-yl]-2-oxo N-(2-oxo-2,3-dihydro-benzothiazol-6-yl) acetamide; or

2-oxo-N-(2-oxo-2,3-dihydro-benzoxazol-6-yl)-2-(4-p-tolyloxy-piperidin-1-yl)-acetamide;

or an optical antipode, racemate or pharmaceutically-acceptable salt thereof.

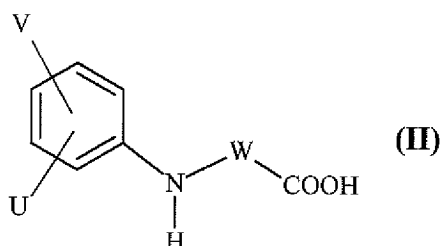
16. (Original) The compound of claim 1 wherein the compound is a functional antagonist of NMDA receptors.

17. (Original) The compound of claim 16 wherein the compound is a functional NR2B subtype specific NMDA receptor antagonist.

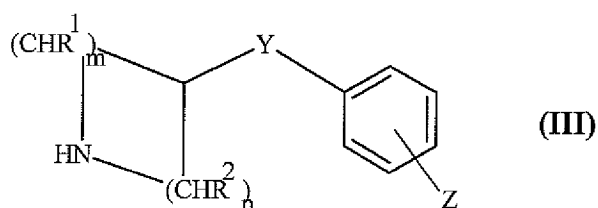
18. (Original) The compound of claim 16 wherein the compound exhibits an IC₅₀ value of less than 54 μ M in a NMDA antagonism or binding test.

19. (Original) The compound of claim 18 wherein the compound exhibits an IC_{50} value of less than $5 \mu M$ in a NMDA antagonism or binding test.

20. (Original) The compound of claim 1, which is synthesized by a method comprising reacting a carboxylic acid of formula (II):

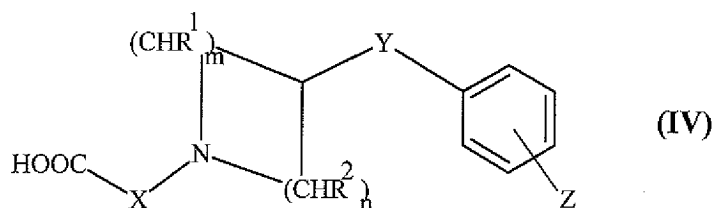


wherein U, V and W are as defined in claim 1, or a reactive derivative thereof, with an amine of formula (III):

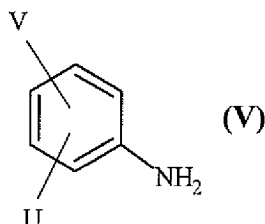


wherein R^1 , R^2 , Y, Z, n and m are as defined in claim 1.

21. (Original) The compound of claim 1, wherein W is -CO-, synthesized by a method comprising reacting a carboxylic acid of formula (IV):

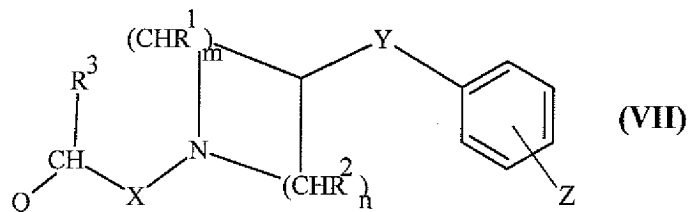


wherein X, R^1 , R^2 , Y, Z, n and m are as defined in claim 1, or a reactive derivative thereof, with an amine of formula (V):

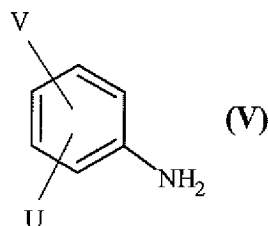


wherein U and V are as defined in claim 1.

22. (Original) The compound of claim 1, wherein W is -CH₂- or -CH₂-(C₁-C₄ alkyl)-, synthesized by a method comprising reacting a halogen derivative of formula (VII):

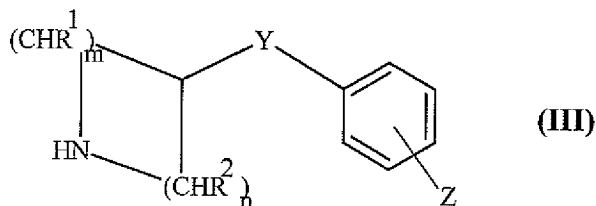


wherein Q is halogen, R³ is hydrogen atom or a C₁-C₄ alkyl and X, R¹, R², Y, Z, n and m are as defined in claim 1 with an amine of formula (V):

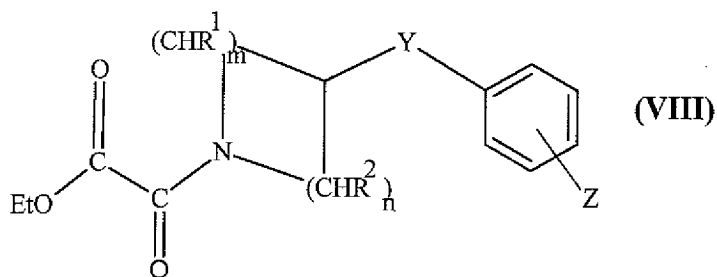


wherein U and V are as defined in claim 1.

23. (Original) The compound of claim 1 synthesized by a method comprising reacting a secondary amine of formula (III):

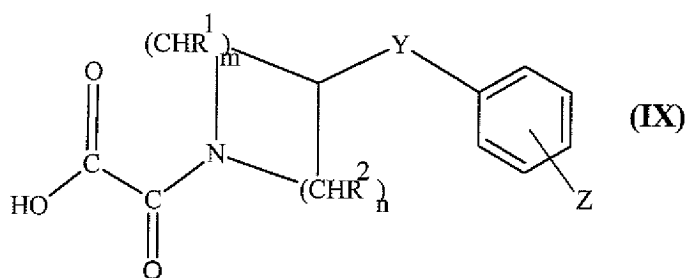


where R¹, R², m, n, Y and Z are as defined in claim 1 with ethyl oxalylchloride in the presence of a solid-supported base in dichloromethane to produce an ester compound of formula (VIII):



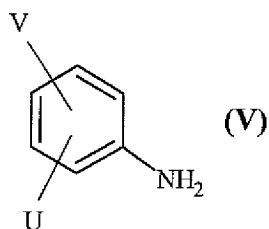
wherein R^1 , R^2 , m , n , Y and Z are as defined as in claim 1;

saponifying the ester compound of formula (VIII) with a strongly basic ion exchange resin in ethanol to produce an oxalamid acid of formula (IX):



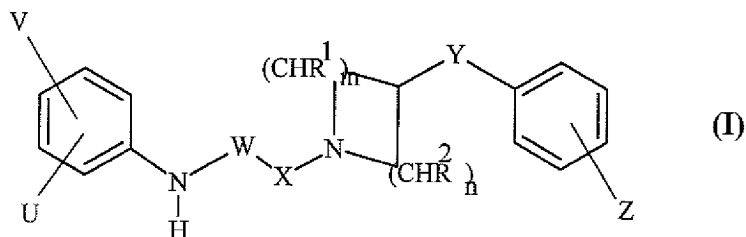
where R^1 , R^2 , m , n , Y and Z are as defined in claim 1; and

reacting the oxalamid acid of formula (IX) with an amide of formula (V):



wherein U and V are as defined in claim 1 in a mixture of dichloromethane and dimethylformamide in the presence of 1-[3-(dimethylamino)-propyl]-3-ethylcarbodiimide to produce the compound of claim 1.

24. (Currently Amended) A pharmaceutical composition comprising a biologically effective dose of a compound of formula (1):



wherein:

V and U: ~~independently are hydrogen, halogen, hydroxyl, cyano, nitro, amino, C₁-C₄-alkylamino, halogen substituted C₁-C₄-alkylamino, arylamino, halogen substituted arylamino, aralkylamino, halogen substituted aralkylamino, C₁-C₄-alkylsulfonamido, halogen substituted C₁-C₄-alkylsulfonamido, C₁-C₄-alkanoylamido, halogen substituted C₁-C₄-alkanoylamido, arylsulfonamido, C₁-C₄-alkylsulfonyloxy, carboxyl, carbamoyl, trifluoromethyl, trifluoromethoxy, C₁-C₄-alkyl-SO₂-NH-CH₂-, C₁-C₄-alkyl-SO₂-NH-, NH₂-(CH₂)₁₋₄-SO₂-NH-, NH₂-(CH₂)₁₋₄-(CO)-NH-, NH₂-SO₂-, CHO-, CH₂-NH₂-, hydroxymethyl, C₁-C₄-alkyl, C₁-C₄-alkoxy methyl, halogenmethyl, tetrazolyl, C₁-C₄-alkoxy, amino substituted C₁-C₄-alkoxy, C₁-C₄-alkoxycarbonyl, amino substituted C₁-C₄-alkoxycarbonyl, C₁-C₆-alkanoyloxy, amino substituted C₁-C₆-alkanoyloxy, phenyl, amino substituted phenyl or acetylamino; or~~

together form a group that contains one or more heteroatoms, and that taken together with one or more:

- (a) hydrogen atoms;
- (b) carbon atoms;
- (c) -CH= groups;
- (d) -CH₂- groups; or
- (e) additional heteroatoms of the same or different type;

or any combination thereof, form a 4-7 membered homocyclic or heterocyclic ring, wherein the homocyclic or heterocyclic ring may combine with the phenyl group to form a bicyclic ring, and wherein the homocyclic or heterocyclic ring or the bicyclic ring may contain one or more oxo, thioxo, amino, mercapto, trifluoromethyl, C₁-C₄ alkyl, =S or -SH groups;

W: is -CO-, -CH₂- or -CH₂-(C₁-C₄ alkyl)-;

X: is -CO-;

Y: is -O-, C₁-C₄ alkylene, C₁-C₄ alkynylene, cycloalkylene, aminocarbonyl, -NH-, -N(C₁-C₄ alkyl)-, -C₁-C₄ alkylene-N(C₁-C₄ alkyl)-, -CH₂O-, -CH(OH)- or -OCH₂-;

Z: is hydrogen, halogen, nitro, amino, C₁-C₄ alkyl, C₁-C₄ alkoxy, cyano, trifluoromethyl, hydroxyl or carboxyl;

R¹ and R²: are hydrogen, or together form a C₁-C₃ bridge; and

n and m: independently are 0-3, wherein n and m cannot each be 0;

or an optical antipode, racemate or pharmaceutically-acceptable salt thereof, and one or more pharmaceutical carriers.

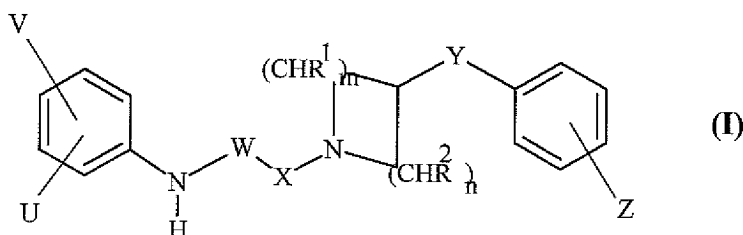
25. (Original) The pharmaceutical composition of claim 24 wherein the compound is a functional antagonist of NMDA receptors.

26. (Original) The pharmaceutical composition of claim 25 wherein the compound is a functional NR2B subtype specific NMDA receptor antagonist.

27. (Original) The pharmaceutical composition of claim 24 wherein the pharmaceutical composition contains 0.01 to 100 mg of the compound in a single dosage unit.

28. (Original) The pharmaceutical composition of claim 24 wherein the pharmaceutical composition is in the form of a tablet.

29. (Currently Amended) A process for synthesizing a compound of formula (I):



wherein:

V and U: independently are hydrogen, halogen, hydroxyl, cyano, nitro, amino, C₁-C₄-alkylamino, halogen substituted C₁-C₄-alkylamino, arylamino, halogen substituted arylamino, aralkylamino, halogen substituted aralkylamino, C₁-C₄ alkylsulfonamido, halogen substituted C₁-C₄ alkylsulfonamido, C₁-C₄ alkanoylamido, halogen substituted C₁-C₄ alkanoylamido, arylsulfonamido, C₁-C₄ alkylsulfonyloxy, carboxyl, carbamoyl, trifluoromethyl, trifluoromethoxy, C₁-C₄ alkyl-SO₂-NH-CH₂-, C₁-C₄ alkyl-SO₂-NH-, NH₂-(CH₂)₁₋₄-SO₂-NH-, NH₂-(CH₂)₁₋₄-(CO)-NH-, NH₂-SO₂-, -CHO-, -CH₂-NH₂-, hydroxymethyl, C₁-C₄-alkyl, C₁-C₄-alkoxy methyl, halogenmethyl, tetrazolyl, C₁-C₄ alkoxy, amino substituted C₁-C₄-alkoxy, C₁-C₄-alkoxycarbonyl, amino substituted C₁-C₄ alkoxy carbonyl, C₁-C₆-alkanoyloxy, amino substituted C₁-C₆-alkanoyloxy, phenyl, amino substituted phenyl or acetylamino; or

together form a group that contains one or more heteroatoms, and that taken together with one or more:

(a) hydrogen atoms;

- (b) carbon atoms;
- (c) -CH= groups;
- (d) -CH₂- groups; or
- (e) additional heteroatoms of the same or different type;

or any combination thereof, form a 4-7 membered homocyclic or heterocyclic ring, wherein the homocyclic or heterocyclic ring may combine with the phenyl group to form a bicyclic ring, and wherein the homocyclic or heterocyclic ring or the bicyclic ring may contain one or more oxo, thioxo, amino, mercapto, trifluoromethyl, C₁-C₄ alkyl, =S or -SH groups;

W: is -CO-, -CH₂- or -CH₂-(C₁-C₄ alkyl)-;

X: is -CO-;

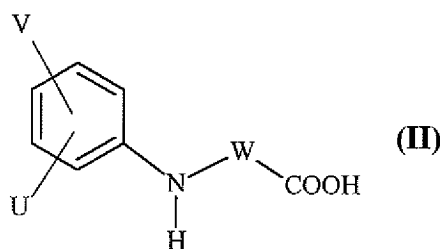
Y: is -O-, C₁-C₄ alkylene, C₁-C₄ alkynylene, cycloalkylene, aminocarbonyl, -NH-, -N(C₁-C₄ alkyl)-, -C₁-C₄ alkylene-N(C₁-C₄ alkyl)-, -CH₂O-, -CH(OH)- or -OCH₂-;

Z: is hydrogen, halogen, nitro, amino, C₁-C₄ alkyl, C₁-C₄ alkoxy, cyano, trifluoromethyl, hydroxyl or carboxyl;

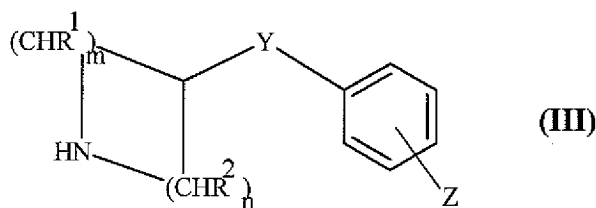
R¹ and R²: are hydrogen, or together form a C₁-C₃ bridge; and

n and m: independently are 0-3, wherein n and m cannot each be 0;

or an optical antipode, racemate or pharmaceutically-acceptable salt thereof, comprising: reacting a carboxylic acid of formula (II):



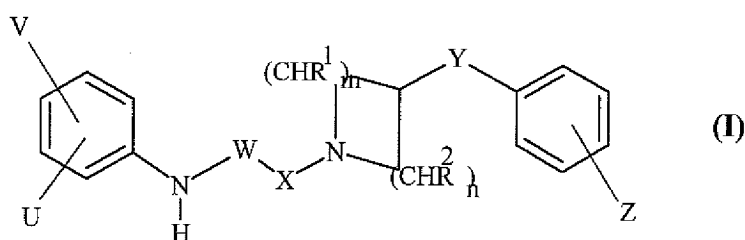
wherein U, V and W are as defined above, or a reactive derivative thereof, with an amine of formula (III):



wherein R^1 , R^2 , Y, Z, n and m are as defined above.

30. (Original) The process of claim 29 wherein the reactive derivative of the carboxylic acid of formula (II) is formed using O-benzotriazol-1-yl-N,N,N',N' tetramethyluronium hexafluorophosphate.

31. (Currently Amended) A process for synthesizing a compound of formula (I):



wherein:

V and U: ~~independently are hydrogen, halogen, hydroxyl, cyano, nitro, amino, C₁-C₄-alkylamino, halogen-substituted C₁-C₄-alkylamino, arylamino, halogen-substituted arylamino, aralkylamino, halogen-substituted aralkylamino, C₁-C₄-alkylsulfonamido, halogen-substituted C₁-C₄-alkylsulfonamido, C₁-C₄-alkanoylamido, halogen-substituted C₁-C₄-alkanoylamido, arylsulfonamido, C₁-C₄-alkylsulfonyloxy, carboxyl, carbamoyl, trifluoromethyl, trifluoromethoxy, C₁-C₄-alkyl-SO₂-NH-CH₂-, C₁-C₄-alkyl-SO₂-NH-, NH₂-(CH₂)₁₋₄-SO₂-NH-, NH₂-(CH₂)₁₋₄-(CO)-NH-, NH₂-SO₂-, -CHO, -CH₂-NH₂, hydroxymethyl, C₁-C₄-alkyl, C₁-C₄-alkoxy-methyl, halogenmethyl, tetrazolyl, C₁-C₄-alkoxy, amino-substituted C₁-C₄-alkoxy, C₁-C₄-alkoxycarbonyl, amino-substituted C₁-C₄-alkoxycarbonyl, C₁-C₆-alkanoyloxy, amino-substituted C₁-C₆-alkanoyloxy, phenyl, amino-substituted phenyl or acetylamino; or~~

together form a group that contains one or more heteroatoms, and that taken together with one or more:

- (a) hydrogen atoms;
- (b) carbon atoms;
- (c) -CH= groups;

(d) -CH₂- groups; or

(e) additional heteroatoms of the same or different type;

or any combination thereof, form a 4-7 membered homocyclic or heterocyclic ring, wherein the homocyclic or heterocyclic ring may combine with the phenyl group to form a bicyclic ring, and wherein the homocyclic or heterocyclic ring or the bicyclic ring may contain one or more oxo, thioxo, amino, mercapto, trifluoromethyl, C₁-C₄ alkyl, =S or -SH groups;

W: is -CO-, -CH₂- or -CH₂-(C₁-C₄ alkyl)-;

X: is -CO-;

Y: is -O-, C₁-C₄ alkylene, C₁-C₄ alkynylene, cycloalkylene, aminocarbonyl, -NH-, -N(C₁-C₄ alkyl)-, -C₁-C₄ alkylene-N(C₁-C₄ alkyl)-, -CH₂O-, -CH(OH)- or -OCH₂-;

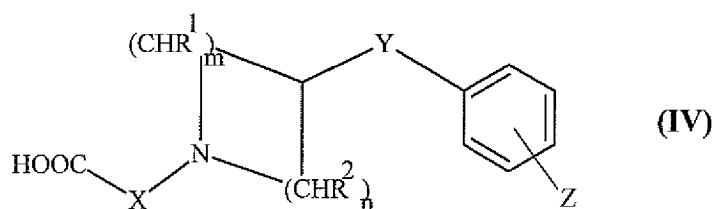
Z: is hydrogen, halogen, nitro, amino, C₁-C₄ alkyl, C₁-C₄ alkoxy, cyano, trifluoromethyl, hydroxyl or carboxyl;

R¹ and R²: are hydrogen, or together form a C₁-C₃ bridge; and

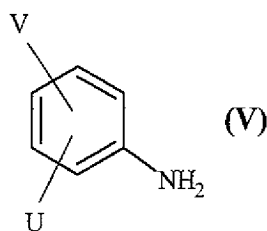
n and m: independently are 0-3, wherein n and m cannot each be 0;

or an optical antipode, racemate or pharmaceutically-acceptable salt thereof, comprising:

reacting a carboxylic acid of formula (IV):



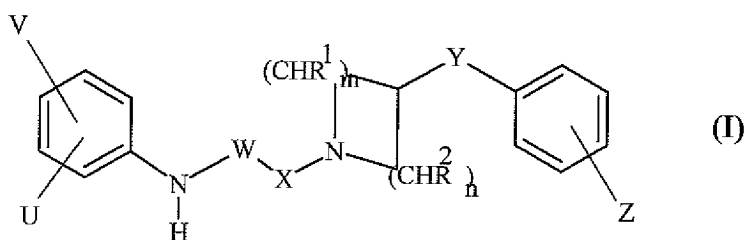
wherein X, R¹, R², Y, Z, n and m are as defined above, or a reactive derivative thereof, with an amine of formula (V):



wherein U and V are as defined above.

32. (Original) The process of claim 31 wherein the reactive derivative of the carboxylic acid of formula (IV) is formed using O-benzotriazol-1-yl-N,N,N,N-tetramethyluronium hexafluorophosphate.

33. (Currently Amended) A process for synthesizing a compound of formula (I):



wherein:

V and U: ~~independently are hydrogen, halogen, hydroxyl, cyano, nitro, amino, C₁-C₄-alkylamino, halogen substituted C₁-C₄-alkylamino, arylamino, halogen substituted arylamino, aralkylamino, halogen substituted aralkylamino, C₁-C₄-alkylsulfonamido, halogen substituted C₁-C₄-alkylsulfonamido, C₁-C₄-alkanoylamido, halogen substituted C₁-C₄-alkanoylamido, arylsulfonamido, C₁-C₄-alkylsulfonyloxy, carboxyl, carbamoyl, trifluoromethyl, trifluoromethoxy, C₁-C₄-alkyl-SO₂-NH-CH₂-, C₁-C₄-alkyl-SO₂-NH-, NH₂-(CH₂)₁₋₄-SO₂-NH-, NH₂-(CH₂)₁₋₄-(CO)-NH-, NH₂-SO₂-, CHO-, CH₂-NH₂-, hydroxymethyl, C₁-C₄-alkyl, C₁-C₄-alkoxy methyl, halogenmethyl, tetrazolyl, C₁-C₄-alkoxy, amino-substituted C₁-C₄-alkoxy, C₁-C₄-alkoxycarbonyl, amino-substituted C₁-C₄-alkoxycarbonyl, C₁-C₆-alkanoyloxy, amino-substituted C₁-C₆-alkanoyloxy, phenyl, amino substituted phenyl or acetylamino; or~~

together form a group that contains one or more heteroatoms, and that taken together with one or more:

- (a) hydrogen atoms;
- (b) carbon atoms;
- (c) -CH= groups;
- (d) -CH₂- groups; or
- (e) additional heteroatoms of the same or different type;

or any combination thereof, form a 4-7 membered homocyclic or heterocyclic ring, wherein the homocyclic or heterocyclic ring may combine with the phenyl group to form a bicyclic ring, and wherein the homocyclic or heterocyclic ring or the bicyclic ring may contain one or more oxo, thioxo, amino, mercapto, trifluoromethyl, C₁-C₄ alkyl, =S or -SH groups;

W: is -CO-, -CH₂- or -CH₂-(C₁-C₄ alkyl)-;

X: is -CO-;

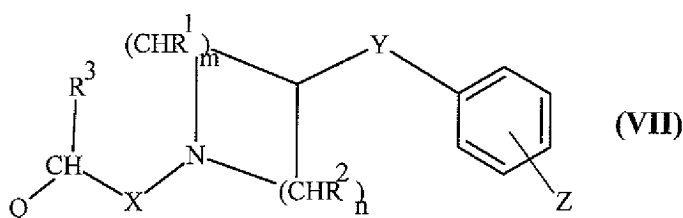
Y: is -O-, C₁-C₄ alkylene, C₁-C₄ alkynylene, cycloalkylene, aminocarbonyl, -NH-, -N(C₁-C₄ alkyl)-, -C₁-C₄ alkylene-N(C₁-C₄ alkyl)-, -CH₂O-, -CH(OH)- or -OCH₂-;

Z: is hydrogen, halogen, nitro, amino, C₁-C₄ alkyl, C₁-C₄ alkoxy, cyano, trifluoromethyl, hydroxyl or carboxyl;

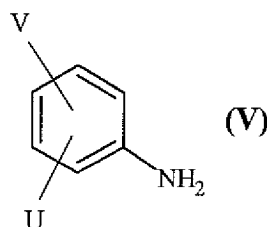
R¹ and R²: are hydrogen, or together form a C₁-C₃ bridge; and

n and m: independently are 0-3, wherein n and m cannot each be 0;

or an optical antipode, racemate or pharmaceutically-acceptable salt thereof, comprising:
reacting a halogen derivative of formula (VII):

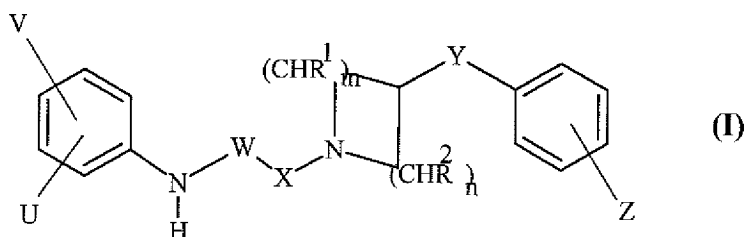


wherein Q is halogen, R³ is hydrogen or a C₁-C₄ alkyl and X, R¹, R², Y, Z, n and m are as defined above with an amine of formula (V):



wherein U and V are as defined above.

34. (Currently Amended) A process for synthesizing a compound of formula (1):



wherein:

V and U: independently are hydrogen, halogen, hydroxyl, cyano, nitro, amino, C₁-C₄-alkylamino, halogen substituted C₁-C₄-alkylamino, arylamino, halogen substituted arylamino, aralkylamino, halogen substituted aralkylamino, C₁-C₄-alkylsulfonamido, halogen substituted C₁-C₄-alkylsulfonamido, C₁-C₄-alkanoylamido, halogen substituted C₁-C₄-alkanoylamido, arylsulfonamido, C₁-C₄-alkylsulfonyloxy, carboxyl, carbamoyl, trifluoromethyl, trifluoromethoxy, C₁-C₄-alkyl-SO₂-NH-CH₂-, C₁-C₄-alkyl-SO₂-NH-, NH₂-(CH₂)₁₋₄-SO₂-NH-, NH₂-(CH₂)₁₋₄-(CO)-NH-, NH₂-SO₂-, -CHO-, -CH₂-NH₂-, hydroxymethyl-, C₁-C₄-alkyl-, C₁-C₄-alkoxy methyl-, halogenmethyl-, tetrazolyl-, C₁-C₄-alkoxy, amino substituted C₁-C₄-alkoxy, C₁-C₄-alkoxycarbonyl, amino substituted C₁-C₄-alkoxycarbonyl, C₁-C₆-alkanoyloxy, amino substituted C₁-C₆-alkanoyloxy, phenyl, amino substituted phenyl or acetylamino; or

together form a group that contains one or more heteroatoms, and that taken together with one or more:

- (a) hydrogen atoms;
- (b) carbon atoms;
- (c) -CH= groups;
- (d) -CH₂- groups; or
- (e) additional heteroatoms of the same or different type;

or any combination thereof, form a 4-7 membered homocyclic or heterocyclic ring, wherein the homocyclic or heterocyclic ring may combine with the phenyl group to form a bicyclic ring, and wherein the homocyclic or heterocyclic ring or the bicyclic ring may contain one or more oxo, thioxo, amino, mercapto, trifluoromethyl, C₁-C₄ alkyl, =S or -SH groups;

W: is -CO-, -CH₂- or -CH₂-(C₁-C₄ alkyl)-;

X: is -CO-;

Y: is -O-, C₁-C₄ alkylene, C₁-C₄ alkynylene, cycloalkylene, aminocarbonyl, -NH-, -N(C₁-C₄ alkyl)-, -C₁-C₄ alkylene-N(C₁-C₄ alkyl)-, -CH₂O-, -CH(OH)- or -OCH₂-;

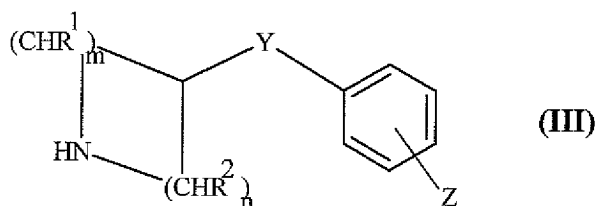
Z: is hydrogen, halogen, nitro, amino, C₁-C₄ alkyl, C₁-C₄ alkoxy, cyano, trifluoromethyl, hydroxyl or carboxyl;

R¹ and R²: are hydrogen, or together form a C₁-C₃ bridge; and

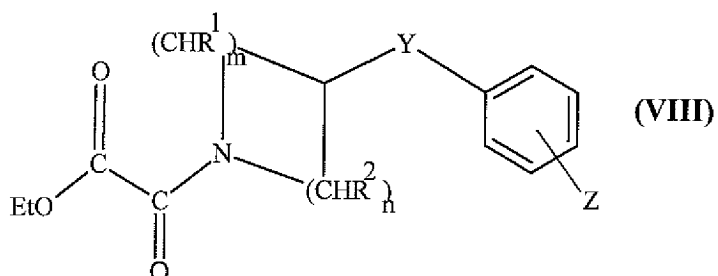
n and m: independently are 0-3, wherein n and m cannot each be 0;

or an optical antipode, racemate or pharmaceutically-acceptable salt thereof, comprising:

reacting a secondary amine of formula (III):

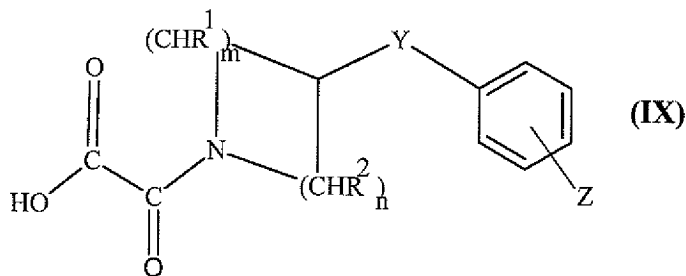


where R¹, R², m, n, Y and Z are as defined above with ethyl oxalylchloride in the presence of a solid-supported base in dichloromethane to produce an ester compound of formula (VIII):



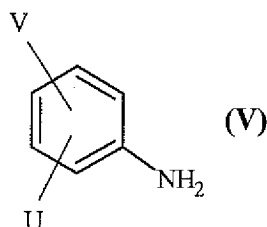
wherein R¹, R², m, n, Y and Z are as defined above,

saponifying the ester compound of formula (VIII) with a strongly basic ion exchange resin in ethanol to produce an oxalamid acid of formula (IX):



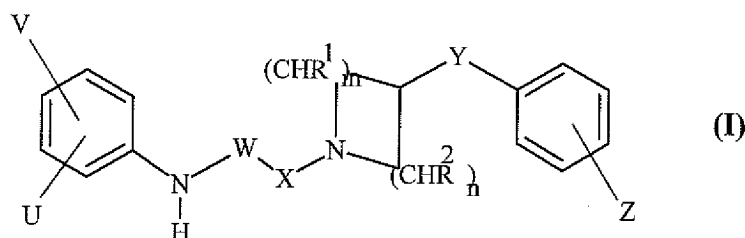
where R¹, R², m, n, Y and Z are as defined above, and

reacting the oxalamid acid of formula (IX) with an amide of formula (V):



wherein U and V are as defined above in a mixture of dichloromethane and dimethylformamide in the presence of 1-[3-(dimethylamino)-propyl]-3-ethylcarbodiimide to produce the compound of claim 1.

35. (Currently Amended) A process for manufacturing pharmaceutical compositions comprising mixing a compound of formula (1):



wherein:

V and U: ~~independently are hydrogen, halogen, hydroxyl, cyano, nitro, amino, C₁-C₄ alkylamino, halogen-substituted C₁-C₄ alkylamino, arylamino, halogen-substituted arylamino, aralkylamino, halogen-substituted aralkylamino, C₁-C₄ alkylsulfonamido, halogen-substituted C₁-C₄ alkylsulfonamido, C₁-C₄ alkanoylamido, halogen-substituted C₁-C₄ alkanoylamido, arylsulfonamido, C₁-C₄ alkylsulfonyloxy, carboxyl, carbamoyl, trifluoromethyl, trifluoromethoxy, C₁-C₄ alkyl-SO₂-NH-CH₂, C₁-C₄ alkyl-SO₂-NH-, NH₂-(CH₂)₁₋₄-SO₂-NH-, NH₂-(CH₂)₁₋₄-(CO)-NH-, NH₂-SO₂-, -CHO, -CH₂-NH₂, hydroxymethyl, C₁-C₄-alkyl, C₁-C₄-alkoxy-methyl, halogenmethyl, tetrazolyl, C₁-C₄ alkoxy, amino-substituted C₁-C₄-alkoxy, C₁-C₄-alkoxycarbonyl, amino-substituted C₁-C₄ alkoxy-carbonyl, C₁-C₆-alkanoyloxy, amino-substituted C₁-C₆-alkanoyloxy, phenyl, amino-substituted phenyl or acetylamino; or~~

together form a group that contains one or more heteroatoms, and that taken together with one or more:

- (a) hydrogen atoms;
- (b) carbon atoms;
- (c) -CH= groups;

(d) -CH₂- groups; or

(e) additional heteroatoms of the same or different type;

or any combination thereof, form a 4-7 membered homocyclic or heterocyclic ring, wherein the homocyclic or heterocyclic ring may combine with the phenyl group to form a bicyclic ring, and wherein the homocyclic or heterocyclic ring or the bicyclic ring may contain one or more oxo, thioxo, amino, mercapto, trifluoromethyl, C₁-C₄ alkyl, =S or -SH groups;

W: is -CO-, -CH₂- or -CH₂-(C₁-C₄ alkyl)-;

X: is -CO-;

Y: is -O-, C₁-C₄ alkylene, C₁-C₄ alkynylene, cycloalkylene, aminocarbonyl, -NH-, -N(C₁-C₄ alkyl)-, -C₁-C₄ alkylene-N(C₁-C₄ alkyl)-, -CH₂O-, -CH(OH)- or -OCH₂-;

Z: is hydrogen, halogen, nitro, amino, C₁-C₄ alkyl, C₁-C₄ alkoxy, cyano, trifluoromethyl, hydroxyl or carboxyl;

R¹ and R²: are hydrogen, or together form a C₁-C₃ bridge; and

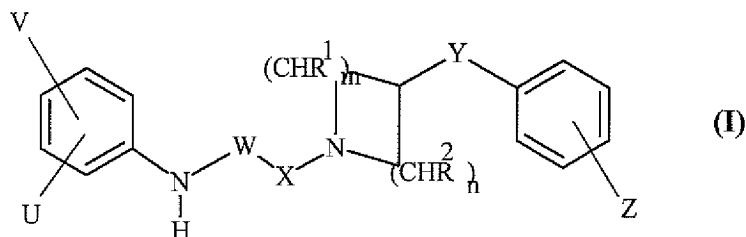
n and m: independently are 0-3, wherein n and m cannot each be 0;

or an optical antipode, racemate or pharmaceutically-acceptable salt thereof, with a pharmaceutical carrier.

36. (Original) The process of claim 35 wherein the compound is a functional NR2B subtype specific NMDA receptor antagonist.

37. (Original) The compound of claim 1 wherein the compound is employed to alleviate a symptom of a disease or disorder in a mammal by administering the compound, or an optical antipode, racemate or pharmaceutically-acceptable salt thereof, to the mammal in an amount effective for alleviating at least one symptom of the disease or disorder, wherein the disease or disorder is a traumatic injury of a brain or spinal cord, human immunodeficiency virus related neuronal injury, amyotrophic lateral sclerosis, tolerance or dependence to opioid pain treatment, withdrawal syndromes from alcohol, opioids or cocaine, ischemic CNS disorders, chronic neurodegenerative disorders, Alzheimers disease, Parkinson's disease, Huntington's disease, pain, epilepsy, anxiety, depression, migraine, psychosis, muscular spasm, dementia, hypoglycemia, degenerative disorders of the retina, glaucoma, asthma, tinnitus or hearing loss.

38. (Withdrawn and Currently Amended) A method for alleviating a symptom of a disease or disorder in a mammal comprising administering to the mammal a compound of formula (I):



wherein:

V and U: independently are hydrogen, halogen, hydroxyl, cyano, nitro, amino, C₁-C₄ alkylamino, halogen substituted C₁-C₄ alkylamino, arylamino, halogen substituted arylamino, aralkylamino, halogen substituted aralkylamino, C₁-C₄ alkylsulfonamido, halogen substituted C₁-C₄ alkylsulfonamido, C₁-C₄ alkanoylamido, halogen substituted C₁-C₄ alkanoylamido, arylsulfonamido, C₁-C₄ alkylsulfonyloxy, carboxyl, carbamoyl, trifluoromethyl, trifluoromethoxy, C₁-C₄ alkyl SO₂-NH-CH₂-, C₁-C₄ alkyl SO₂-NH-, NH₂-(CH₂)₁₋₄-SO₂-NH-, NH₂-(CH₂)₁₋₄-(CO)-NH-, NH₂-SO₂-, CHO-, CH₂-NH₂-, hydroxymethyl, C₁-C₄ alkyl, C₁-C₄ alkoxy methyl, halogenmethyl, tetrazolyl, C₁-C₄ alkoxy, amino substituted C₁-C₄ alkoxy, C₁-C₄ alkoxy carbonyl, amino substituted C₁-C₄ alkoxy carbonyl, C₁-C₆ alkanoyloxy, amino substituted C₁-C₆ alkanoyloxy, phenyl, amino substituted phenyl or acetylamino; or

together form a group that contains one or more heteroatoms, and that taken together with one or more:

- (a) hydrogen atoms;
- (b) carbon atoms;
- (c) -CH= groups;
- (d) -CH₂- groups; or
- (e) additional heteroatoms of the same or different type;

or any combination thereof, form a 4-7 membered homocyclic or heterocyclic ring, wherein the homocyclic or heterocyclic ring may combine with the phenyl group to form a bicyclic ring, and wherein the homocyclic or heterocyclic ring or the bicyclic ring may contain one or more oxo, thioxo, amino, mercapto, trifluoromethyl, C₁-C₄ alkyl, =S or -SH groups;

W: is -CO-, -CH₂- or -CH₂-(C₁-C₄ alkyl)-;

X: is -CO-;

Y: is -O-, C₁-C₄ alkylene, C₁-C₄ alkynylene, cycloalkylene, aminocarbonyl, -NH-, -N(C₁-C₄ alkyl)-, -C₁-C₄ alkylene-N(C₁-C₄ alkyl)-, -CH₂O-, -CH(OH)- or -OCH₂-;

Z: is hydrogen, halogen, nitro, amino, C₁-C₄ alkyl, C₁-C₄ alkoxy, cyano, trifluoromethyl, hydroxyl or carboxyl;

R¹ and R²: are hydrogen, or together form a C₁-C₃ bridge; and

n and m: independently are 0-3, wherein n and m cannot each be 0;

or an optical antipode, racemate or pharmaceutically-acceptable salt thereof,
wherein the compound of formula (I) is administered in an amount effective for alleviating at least one symptom of the disease or disorder, and

wherein the disease or disorder is a traumatic injury of a brain or spinal cord, human immunodeficiency virus related neuronal injury, amyotrophic lateral sclerosis, tolerance or dependence to opioid pain treatment, withdrawal syndromes from alcohol, opioids or cocaine, ischemic CNS disorders, chronic neurodegenerative disorders, Alzheimer's disease, Parkinson's disease, Huntington's disease, pain, epilepsy, anxiety, depression, migraine, psychosis, muscular spasm, dementia, hypoglycemia, degenerative disorders of the retina, glaucoma, asthma, tinnitus or hearing loss.